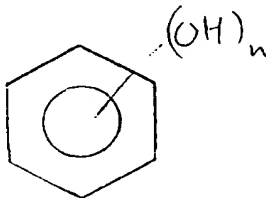


CLAIMS

1. A chemical composition having oxygen transporting capability and comprising biocompatible oxygen transporting molecules chemically bonded to one or more biocompatible antioxidants selected from phenolic compounds; pyrazolines; carotenoid and retinoid compounds; quinones; tetrapyrroles; indoles and aminoindoles; purine analogs; ascorbic acid; and steroid and alkaloid antioxidants.

2. The chemical composition of claim 1 wherein the antioxidant is a phenolic compound containing one or more groups of formula:



where n is an integer from 1 - 3, the aromatic ring being further substituted, and being optionally fused or linked to another carbocyclic or heterocyclic ring system.

3. The chemical composition of claim 2 wherein the phenolic compound is a polyphenolic, a substituted phenolic, phenolic ethers; di-tert.butylhydroxyphenylthio-substituted hydroxamic acids; chroman-based compounds such as chromanols and dihydrobenzofuranols; flavanoids and isoflavanoids such as flavanone and dihydroflavanol; gallates; catechols and catechol derivatives; and phenolic acids.

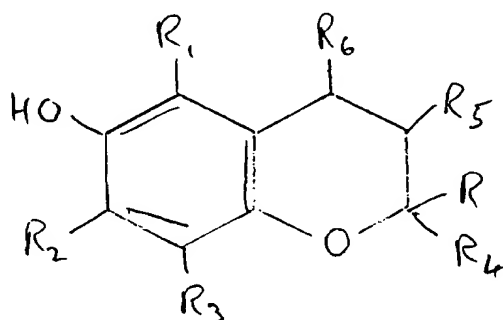
4. The chemical composition of claim 3 wherein the phenolic

antioxidant is a chromanol.

5. The chemical composition of claim 3 wherein the oxygen transporting substance is a heme-protein macromolecule.

6. The chemical composition of claim 5 wherein the heme-protein macromolecule is a hemoglobin species.

7. A chemical composition according to claim 1 consisting essentially of an oxygen transporting compound and a 6-hydroxy chroman compound having antioxidant properties and corresponding to the general formula:



where each of R₁, R₂ and R₃ is independently selected from H, C₁ - C₈ alkyl and (CH₂)_nX where n is an integer from 0 to 20; each of R₄, R₅ and R₆ is independently selected from H, C₁ - C₂₀ alkyl, X and -(CH₂)_mX where m is an integer from 0 - 20; and X is a reactive functional group selected in conjunction with the chosen oxygen transporting compound so as to be reactive therewith to effect chemical linkage of the oxygen transporting compound to the chroman compound; with the proviso that the chroman compound includes at least one functional group X.

8. The chemical composition of claim 7 wherein the oxygen

transporting macromolecule is a heme-protein macromolecule and the functional group X on the chroman compound is a group reactive with amino acid residues of the protein chains thereof.

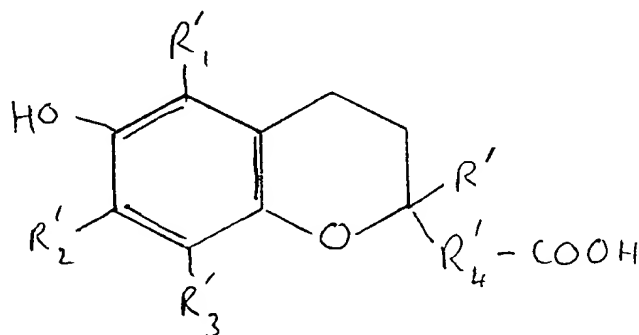
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9. The composition of claim 8 wherein the heme-protein macromolecule is a hemoglobin species and the functional group X is selected from halo, carboxyl, amino, hydroxyl, thiol, azide, azo, aldehyde, guanidine and phosphate.

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10. The composition of claim 9 wherein the chroman compound is a chroman carboxylic acid corresponding to the general formula:

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where R' is H or an alkyl radical of 1-20 carbon atoms or R'1, R'2, and R'3, are independently selected from H and C1-C4 alkyl, and R'4 is a direct bond or C1-8 alkyl chain.

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11. The composition of claim 10 wherein the composition is a covalently linked conjugate of said chroman compound and human hemoglobin.

12. The composition of any of claims 6, 9, 10 or 11

wherein the hemoglobin of the conjugate is cross-linked to form stabilized tetrameric units.

13. The composition of any of claims 6 and 9 - 12 wherein the hemoglobin of the conjugate is at least partially oligomerized into oligomers of up to twelve stabilized tetrameric units.

14. The composition of any of claims 6 and 9 - 13 comprising a mixture of tetrameric stabilized hemoglobin units conjugated to the chroman carboxylic acid antioxidant and oligomers of from 2 - 8 such stabilized hemoglobin units conjugated to the chroman carboxylic acid antioxidant.

15. The composition of any of claims 12 - 14 wherein the hemoglobin is cross-linked with a polyaldehyde, glutaraldehyde, a diaspirin compound, a pyridoxyl compound or a trimesoyl compound.

16. The composition of claim 15 wherein the hemoglobin is cross-linked with a polyaldehyde derived from oxidative ring-opening of a polysaccharide.

17. The composition of claim 16 wherein the polyaldehyde is o-raffinose.

18. The composition of any of claims 6 and 12 - 17 wherein the hemoglobin-antioxidant conjugate is bonded to a biocompatible polymer.

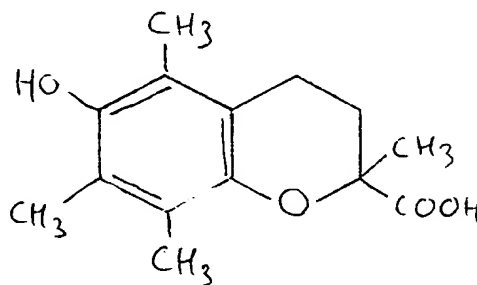
19. The composition of claim 18 wherein the biocompatible polymer is polyethylene glycol, a

polysaccharide, a polyamino acid, or an insoluble support.

20. The composition of claim 10 wherein, in the formula of the chroman carboxylic acid, at least one of R_1 , R_2 and R_3 is methyl.

21. The composition of claim 20 wherein, in the formula of the chroman carboxylic acid, R_4 is a direct bond.

22. The composition of any of claims 7 - 21, wherein the chroman carboxylic antioxidant is Trolox, of formula:



23. A process of preparing a hemoglobin composition having antioxidant properties and suitable for administration to a mammalian patient, which comprises chemically reacting stroma-free hemoglobin and a chroman carboxylic acid as defined in claim 10 with purified, stroma-free hemoglobin to form a covalently linked chemical conjugate thereof.

24. The process of claim 23 wherein the reaction between hemoglobin and chroman carboxylic acid is conducted in the presence of an activating compound.

25. The process of claim 24 wherein, prior to conjugation to the chroman carboxylic acid, the hemoglobin is reacted with a cross-linking reagent to stabilize it in its tetrameric-unit form, against dissociation into dimeric units.

26. The process of claim 25 wherein the cross-linking reagent is a polyaldehyde.

27. The process of claim 26 wherein the polyaldehyde is o-raffinose, and the hemoglobin is additionally at least partially oligomerized by further reaction with o-raffinose.

28. The process of claim 27 wherein the hemoglobin-chroman carboxylic acid conjugate is subsequently reacted with a cross-linking reagent to effect cross-linking stabilization of the hemoglobin portion of the conjugate.

29. The process of claim 28 wherein the cross-linking reagent is o-raffinose.

30. The process of claim 28 wherein the activating compound is a carbodiimide.

31. The process of claim 30 wherein the carbodiimide is 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide.

32. The process of any of claims 24 - 31 wherein the chroman carboxylic acid is 2,5,7,8-tetramethyl-2-

carboxy-chroman-6-ol.

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